Home versus in-patient treatment for deep vein thrombosis

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Authors

Richard Othieno[1], Emmanuel Okpo[2], Rachel Forster[3]

[1]NHS Lothian, Directorate of Public Health and Health Policy, Edinburgh, UK
[2]Public Health Directorate, NHS Grampian, Aberdeen, UK
[3]Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK

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Contact person

Richard Othieno

Consultant in Public Health Medicine
NHS Lothian, Directorate of Public Health and Health Policy
Waverly Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
UK

E-mail: richard.othieno@nhslothian.scot.nhs.uk

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What's new

Date	Event	Description
29 May 2017	New citation: conclusions not changed	Searches re-run. One new study included and five new studies excluded. Review text updated to incorporate updated Cochrane requirements. New headings were added, included studies assessed for risk of bias, GRADE ratings generated and 'Summary of findings' table populated. Conclusions not changed.
29 May 2017	Updated	Searches re-run. One new study included and five new studies excluded.

History

Date	Event	Description
14 February 2011	Amended	Link to anticoagulant feedback added
13 May 2008	Amended	Converted to new review format.
9 November 2007	Updated	No new trials found. One additional secondary reference added to Ramacciotti 2004 (included study). No change to conclusions.
22 May 2007	New citation: conclusions not changed	New team of authors.Two new included trials and six new excluded trials. Overall conclusions strengthened with further evidence.
27 May 2004	Updated	No new trials found. Review updated as it stands.

Abstract

Background

Deep vein thrombosis (DVT) occurs when a blood clot blocks blood flow through a vein, which can occur after surgery, trauma, or when a person has been immobile for a long period of time. Clots can dislodge and block blood flow to the lungs (pulmonary embolism (PE)), causing death. DVT and PE are both known by the term venous thromboembolism (VTE). Heparin (in the form of unfractionated heparin (UFH) is a blood-thinning drug used in the first three to five days of DVT treatment. Low molecular weight heparins (LMWH) allow people with DVT to receive their initial treatment at home instead of in hospital. This is an update of a review first published in 2001 and updated in 2007.

Objectives

To compare the incidence and complications of venous thromboembolism (VTE) in participants treated at home versus participants treated with standard in-patient hospital regimens. Secondary objectives included patient satisfaction and cost effectiveness.

Search methods

For this update, the Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register (last searched 16 March 2017), CENTRAL (2017, Issue 2), and trials registries. We also checked reference lists of relevant publications.

Selection criteria

Randomised controlled trials (RCTs) of home versus hospital treatment for DVT in which DVT was clinically confirmed and treated with either LMWH or UFH.

Data collection and analysis

One review author selected the material for inclusion and another author reviewed the selection of trials. Two review authors independently extracted data and assessed included studies for risk of bias. Primary outcomes included combined VTE events (PE and recurrent DVT), gangrene, heparin complications, and death. Secondary outcomes were patient satisfaction and cost implications. We performed meta-analysis using fixed-effect models with risk ratios (RR) and 95% confidence intervals (CIs) for dichotomous data.

Main results

Seven RCTs involving 1839 randomised participants with comparable treatment arms were included. All seven had fundamental problems including high exclusion rates, partial hospital treatment of many in the home treatment arms, and comparison of UFH in hospital with LMWH at home. The trials showed that patients treated at home with LMWH are less likely to have recurrence of VTE events compared with hospital treatment with UFH or LMWH (fixed effect risk ratio (RR) 0.58, 95% confidence interval (CI) 0.39 to 0.86; 6 studies; 1708 participants; P = 0.007) (low-quality evidence). No clear difference was seen between the groups for major bleeding (RR 0.67; 95% CI 0.33 to 1.36; 6 studies; 1708 participants; P = 0.27) (low-quality evidence), minor bleeding (RR 1.29; 95% CI 0.94 to 1.78; 6 studies; 1708 participants; P = 0.11) (low-quality evidence) or mortality (RR 0.69, 95% CI 0.44 to 1.09; 6 studies; 1708 participants; P = 0.11) (low-quality evidence). There were no reports of venous gangrene in any of the included studies. Patient satisfaction and quality of life outcomes could not be combined in meta-analysis due to heterogeneity of reporting, but two of the three studies found evidence that home treatment had greater improvements in quality of life compared with in-patient treatment at some point during the follow-up, and the third study reported a large number of participants chose to switch from in-patient care to home-based care for social and personal reasons, suggesting it is the patient's preferred option (very low-quality evidence). None of the studies included in the review carried out a full cost effectiveness analysis. However, a small randomised economic evaluation of the two alternative treatment settings involving 131 participants found that direct costs were higher for those in

the in-patient group. These findings were supported by three other studies that reported on costs for their studies (very low-quality evidence).

Quality of evidence of the data from the meta-analyses was low to very low. This was due to risk of bias as many of the included studies had unclear randomisation techniques, and blinding was a concern for many. Also, there was a concern with indirectness as a majority of the studies had a large number of participants who were randomised to the home (LMWH) treatment group that were treated in hospital for some or all of the treatment period. A further issue for some outcomes was heterogeneity in the measurement and reporting of the outcome.

Authors' conclusions

There is low-quality evidence that patients treated at home with LMWH are less likely to have recurrence of VTE compared to those treated in the hospital. However, no clear differences in major or minor bleeding, or for mortality, were seen (low-quality evidence), indicating that home treatment is no worse for these outcomes when compared with in-patient treatment. Further large trials comparing these treatments are unlikely to occur. Therefore, home treatment is likely to become the norm and further research will be directed to resolving practical issues such as developing local guidelines which contain clinical prediction rules, biomarkers and imaging which can be used to tailor therapy to the severity of the disease as well as development of training for community healthcare workers to administer and monitor treatment progress.

Plain language summary

Home versus in-patient treatment for deep vein blood clots

Background

Deep vein thrombosis (DVT) occurs when a blood clot blocks blood flow through a vein, generally in the legs. This can happen after surgery, trauma, when a person is immobile for a long period of time, or for no obvious reason. Clots can dislodge and block blood flow to the lungs (pulmonary embolism (PE)), which can be fatal. DVT and PE are both known as venous thromboembolism (VTE). Heparin is a blood-thinning drug used to treat DVT during the first three to five days. Unfractionated heparin (UFH) is administered intravenously in hospital with laboratory monitoring. Low molecular weight heparins (LMWH) are given by subcutaneous injection once a day and can be given at home. Oral anticoagulants are then continued for three to six months. After recovery from the acute episode, people may develop post-thrombotic syndrome with leg swelling, varicose veins and ulceration.

Study characteristics and key results

Seven randomised controlled trials involving 1839 patients with clinically confirmed DVT compared home (LMWH) versus hospital (heparin, or LMWH in one trial) treatment. Trials had limitations including high exclusion rates and designs that did not take into account short hospital stays for any of the people who were treated at home to allow fair comparison of heparin in hospital with LMWH at home.

The trials showed that patients treated at home with LMWH had a lower recurrence of VTE compared with hospital-treated patients. The review showed no clear difference between the treatment groups for major bleeding, minor bleeding or deaths. No venous gangrene was reported in any study. We could not pool the information on patient satisfaction and quality of life as studies had different ways of reporting these, but two of the three studies reporting on quality of life found evidence that home treatment had greater improvements in quality of life compared with in-patient treatment, at some point during the follow-up. The third study reported a large number of participants chose to switch from in-patient care to home-based care for social and personal reasons, indicating that home treatment was more accepted compared with in-patient treatment. Studies which looked at cost showed that home management had a lower cost per incident of treatment.

Quality of the evidence

Overall, the quality of evidence of the data was low to very low due to risk of bias, indirectness and differences in measuring and reporting of outcomes. Risk of bias is a concern as many of the included studies did not fully explain how they randomised and allocated their participants to the treatments and also blinding techniques were not clear. Full blinding would be difficult if not impossible for these types of treatments (home versus hospital) but there are techniques that could be put in place such a using the same treatment medications and blinding those who measure the outcomes. Another concern was that in some studies, participants randomised to home treatment actually ended up being treated in hospital, but remained in their assigned treatment for the analysis (this is known as indirectness). This makes it hard to determine if the results actually answer the question of whether home versus hospital treatment for DVT is superior. A further concern for a few of the outcomes was variation in the way the outcome was measured and reported.

Background

Description of the condition

Deep vein thrombosis (DVT) is a frequent disorder in western medical practice, affecting one to two per thousand of the adult population annually. DVT occurs in conjunction with malignancy, after surgery, trauma and immobilisation, and can occur spontaneously. It manifests in the acute stage with leg symptoms and, in a small minority, with potentially fatal pulmonary embolism (PE). Venous thromboembolism (VTE) is a term that refers to both DVT and PE. After recovery from the acute episode, people may develop post-thrombotic syndrome with leg swelling, varicosis and ulceration. The gold standard techniques for diagnosing DVT are ascending venography and duplex ultrasound scanning. Deep vein thrombosis is most commonly managed by anticoagulants to prevent spread of the clot proximally and allow it to become adherent or undergo fibrinolysis, thus reducing the risk of PE. Currently used anticoagulant

treatment includes unfractionated and low molecular weight heparin (UFH and LMWH, respectively) as well as vitamin K antagonists (VKA), primarily warfarin, and direct oral anticoagulants (DOACs) (NICE 2012; Robertson 2015; van Es 2014).

Description of the intervention

In the hospitalised patient UFH is usually administered intravenously, with laboratory monitoring for about five days, overlapping with oral anticoagulants that are continued for three to six months. LMWH is administered daily by subcutaneous injection, which can be delivered at home without need for continuous laboratory monitoring, also followed by an oral anticoagulant regimen.

Why it is important to do this review

The development of LMWHs has resulted in many trials investigating their efficaciousness and safety, as compared with UFH. These studies show that LMWH is at least as effective as UFH, with some meta-analyses and reviews showing that LMWH is more effective and safer than UFH (Erkens 2010; Leizorovicz 1994; Lensing 1995). Because LMWH is given subcutaneously once per day and requires no laboratory monitoring it is possible to treat people with LMWH at home. Although LMWH has been available since 1976, home treatment was not investigated further since it was first reported in 1988 (Bakker 1988). Rigorous evaluation is required for the home versus in-patient care to inform policy on alternative strategies for treating DVT. There is potential for home treatment of DVT to save costs and to be more socially acceptable to the patients. This review aims to update the review which was first published in 2001 and updated in 2007 (Othieno 2007).

Objectives

To compare the incidence and complications of venous thromboembolism (VTE) in participants treated at home versus participants treated with standard in-patient hospital regimens. Secondary objectives included patient satisfaction and cost effectiveness.

Methods

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) in which the participants were randomised to home or in-patient treatment. Exclusion criteria before randomisation had to be stated and the author's policy regarding protocol violations and withdrawals known (i.e. intention-to-treat basis).

Types of participants

We included people with proven VTE in whom there was no contraindication to heparin therapy and whose home circumstances were adequate. Participants had to have objective evidence of DVT: the accepted and reliable proofs being duplex scanning and/or venography.

Types of interventions

We included studies that compared home to hospital management with LMWH (which can be used in either setting) or UFH (which is used in hospital only). Trials involving a placebo group are not ethically acceptable.

Types of outcome measures

Primary outcomes

- Recurrence of VTE: PE or recurrence of DVT (depending on the length of follow-up)
- Venous gangrene
- Heparin complications: major and minor bleeding (the former being defined as bleeding within the abdomen, cranium or eye, or requiring transfusion, or causing a fall in haemoglobin of 2 g/dL or greater)
- Death

Ideally, evidence of PE is derived from lung scans, spiral computed tomography (CT) or pulmonary angiography, but as these were not likely to be widely available, X-rays, ECG and strong clinical signs were considered acceptable. In the event of death, post-mortem evidence was desirable.

Secondary outcomes

- Patient satisfaction and quality of life
- Cost effectiveness of treatment (as reported by the individual studies)

We will also report on other outcomes of interest (i.e., post-thrombotic syndrome or length of stay in hospital), when reported in the individual studies.

Search methods for identification of studies

Electronic searches

For this update the Cochrane Vascular Information Specialist (CIS) searched the following databases for relevant trials.

- The Cochrane Vascular Specialised Register (16 March 2017).
- The Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 2) via the Cochrane Register of Studies

Online.

See Appendix 1 for details of the search strategy used for CENTRAL.

The Cochrane Vascular Specialised Register is maintained by the CIS and is constructed from weekly electronic searches of MEDLINE Ovid, Embase Ovid, CINAHL and AMED as well as through handsearching relevant journals. The full list of the databases, journals and conference proceedings searched, as well as the search strategies used, are described in the Specialised Register section of the Cochrane Vascular module in the Cochrane Library (www.cochranelibrary.com).

In addition, the CIS searched the following trial databases for details of ongoing and unpublished studies (16 March 2017). See Appendix 2.

- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal. (apps.who.int/trialsearch)
- ClinicalTrials.gov (clinicaltrials.gov)
- International Standard Randomised Controlled Trial Number (ISRCTN) registry (www.isrctn.com)

Searching other resources

Additional articles were identified by reviewing the references of relevant papers resulting from the initial search.

Data collection and analysis

Selection of studies

For this update, three review authors (RO, EO, RF) independently selected trials. The final selection of articles was agreed by discussion and consensus.

Data extraction and management

Two review authors (RO, EO) independently extracted data from existing and newly included trials using the criteria designed by Cochrane Vascular. For some references, additional clarification was sought from trial authors. Two review authors (RO, EO) performed the data entry.

Assessment of risk of bias in included studies

Two review authors (RO, EO) independently assessed the risk of bias of all the included studies using Cochrane's 'Risk of bias' tool as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assessed the included RCTs against the six domains listed below. We rated studies as having 'low risk of bias' (plausible bias unlikely to seriously alter the results); 'high risk of bias' (plausible bias that seriously weakens confidence in the results); or 'unclear risk of bias' (plausible bias that raises some doubt about results).

- Sequence generation: was the allocation sequence adequately described?
- Allocation concealment: was allocation adequately concealed?
- Blinding of participants, personnel, and outcome assessors: was knowledge of the allocation intervention adequately prevented during the study?
- Incomplete outcome data: was incomplete outcome data adequately addressed?
- Selective outcome reporting: are reports of the study free of suggestion of selective outcome reporting?
- Other sources of bias: did the study appear to be free of other problems that could put it at high risk of bias?

Measures of treatment effect

Two review authors (RO, EO) performed the data analysis. Analyses were performed according to the statistical guidelines for review authors from the Cochrane Vascular Group. Where there were sufficient data, we calculated a risk ratio (RR) with 95% confidence intervals (CI) using Review Manager software (RevMan 2014).

Unit of analysis issues

None of the included studies had non-standard designs, such as cross-over trials or cluster-randomised trials. We therefore did not make any adjustments for measurement effects. The individual participant was the unit of analysis.

Dealing with missing data

We aimed to conduct a complete-case analysis in this Cochrane Review, such that all patients with a recorded outcome were included in the analysis. We analysed data on an intention-to-treat basis as far as possible. Where data were missing, we made attempts to obtain them from the original investigators. Where they were unobtainable, we only analysed the available data, based on the numerator and denominator reported in study results or calculable from reported percentages.

Assessment of heterogeneity

We examined heterogeneity between the trials by visually examining the forest plots to judge whether there were any apparent differences in the direction or size of the treatment effect between studies. We also considered the I^2 and Tau^2 statistics and the P value of the Chi^2 test for heterogeneity. If we identified heterogeneity among the trials (if the value of I^2 was greater than 30%, and the value of Tau^2 was greater than zero or the P value of the Chi^2 test for heterogeneity was lower than 0.1), we planned to explore heterogeneity by pre-specified sensitivity analysis as described below.

Assessment of reporting biases

In view of the difficulty in detecting and correcting for publication bias and other reporting biases, we aimed to minimise their potential impact by ensuring a comprehensive search for eligible studies and by being alert for

duplication of data. We planned to use a funnel plot to assess the possibility of small-study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies) for the primary review outcomes when 10 or more studies were included in the meta-analyses (Higgins 2011). We intended to cautiously consider visible asymmetry in the funnel plot as a possible indication of publication bias.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). We used a fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar.

Random-effects meta-analysis would be used if there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected.

Subgroup analysis and investigation of heterogeneity

If identified, we planned to explore any possible evidence of heterogeneity within the meta-analyses by subgroup analysis. There are no other planned subgroup analyses.

Sensitivity analysis

We performed sensitivity analyses by excluding studies that we judged to be at high risk of bias in order to determine the effect on the overall finding. We also performed sensitivity analysis if a single study carried a majority weight when there were three or more studies included in an analyses. We preformed additional sensitivity analysis to determine the robustness of the findings that included data from Koopman 1996; Levine 1996 and Ramacciotti 2004; as we determined that participants randomised to LMWH were only treated at home as determined by a clinician, and not specifically assigned to home treatment.

Summary of findings

We presented the main findings of the review results concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data for all outcomes of this review (Types of outcome measures) in a 'Summary of findings' table, according to the GRADE principles as described by Higgins 2011 and Atkins 2004. Evidence is evaluated based on risk of bias of the included studies, inconsistency, indirectness and imprecision of the data, as well as publication bias. We used the GRADEprofiler (GRADEpro) software to assist in the preparation of the 'Summary of findings' table (GRADEProGDT 2015). The publication by Ryan 2016 was utilised to prepare the GRADE ratings.

Results

Description of studies

Results of the search

See Figure 1

Included studies

In total, seven studies were eligible for inclusion in this review with a total of 1839 participants (Bäckman 2004; Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). One new study was identified for this review update (Bäckman 2004). This study had previously been excluded on the grounds that it did not assess any of the primary outcomes, but after further assessment we decided it should be included as the study did report on economic data.

Three large trials (Chong 2005; Koopman 1996; Levine 1996) randomised 298 (150 home and 148 hospital), 400 (202 home and 198 hospital), and 500 participants (247 home and 253 hospital) respectively. There were also three smaller trials (Boccalon 2000; Daskalopoulos 2005; Ramacciotti 2004). Boccalon 2000 reported results on 201 randomised participants (99 home and 102 hospital); Ramacciotti 2004 reported results on 104 home and 97 hospital randomised participants and in Daskalopoulos 2005, 108 participants were randomised (55 home and 53 hospital). Bäckman 2004 evaluated and compared direct and indirect medical costs during a three-month period among 131 randomised participants (65 out-patient/home and 66 in-patient).

Bäckman 2004 did not report on any of the predefined outcomes of this review other than costs and is therefore not included in any meta-analyses for these outcomes.

The three major trials (Chong 2005; Koopman 1996; Levine 1996) were similar in construction and results, but differed in their exclusion rates (see Characteristics of included studies; further discussed in Overall completeness and applicability of evidence). Of the seven trials, only Boccalon 2000 and Bäckman 2004 used LMWH in both treatment arms, the other five used LMWH in home-treatment arms and UFH in the hospital-treatment arms.

See Characteristics of included studies tables for further details of the included studies

Excluded studies

For this update an additional five studies were excluded (Aujesky 2011; Hull 2009; Modesto-Alapont 2006; Otero 2010; Wilson 2003). In total 26 studies were excluded (Aujesky 2011; Belcaro 1999; Blattler 1998; Buller 2004; Conner 1999; Fitzmaurice 2000; Frank 1998; Goldhaber 1998; Grau 1998; Grau 2001; Green 1998; Hull 2000; Hull 2002; Hull 2009;

Lindmarker 1996; Miles 1998; Modesto-Alapont 2006; O'Shaugnessy 1998; Otero 2010; Pineo 2003; Rymes 2002; Ting 1998; Wells 1998; White 1989; Wilson 2003; Wimperis 1998).

Eight were uncontrolled studies (Conner 1999; Grau 1998; Green 1998; Lindmarker 1996; Miles 1998; O'Shaugnessy 1998; Ting 1998; Wimperis 1998). Two trials were retrospective studies (Grau 2001; Rymes 2002). The remaining 16 trials were excluded for a variety of reasons. Two reported controlled trials were excluded because participants were not actually randomised but instead treated according to their expressed therapeutic preferences (Blattler 1998; Frank 1998). Wells 1998 was excluded because it compared patient-administered with nurse-administered injections rather than the location of treatment. Goldhaber 1998 was excluded because participants randomised to treatment with LMWH in a home setting were first required to be treated in hospital for a number of days. Otero 2010 and Aujesky 2011 focused on PE and not DVT. Belcaro 1999 was excluded because it was primarily a trial of formulations of heparin rather than a trial of home versus hospital treatment. Hull 2000 and Modesto-Alapont 2006 were excluded because they were concerned with prophylactic regimens using LMWH in patients undergoing hip arthroplasty and those with VTE in obstructive pulmonary disease, respectively. Pineo 2003 and Hull 2002 were excluded because they investigated two protocols of long-term effects of LMWH treatment and not location. Two other excluded trials did not have in-patient arms, Wilson 2003 compared anticoagulant clinics and family clinics, while Hull 2009 compared long-term subcutaneous tinzaparin with initial tinzaparin followed by long-term warfarin in the community as opposed to home versus inpatients. White 1989 and Fitzmaurice 2000 were concerned with the monitoring of oral anticoagulation at home or in the GP surgery. Buller 2004 compared once daily LMWH with twice daily doses in the out-patient setting and LMWH with UFH in out-patient setting and not hospital versus home.

See also Characteristics of excluded studies.

Risk of bias in included studies

Figure 2 gives an overall view of our assessment of the included studies' risk of bias while Figure 3 shows the 'Risk of bias' summary presented as percentages across all included studies. See also Characteristics of included studies.

Allocation (selection bias)

We considered the following methods of allocation concealment adequate:

- central allocation, including telephone randomisation;
- sequentially numbered, opaque, sealed envelopes.

We deemed the risk of bias low if one of these methods was described. We deemed the risk of bias unclear if the study was described as randomised but the method used for allocation concealment was not described.

All the included trials were reported as randomised controlled trials (RCTs). Random sequence generation was unclear in six studies (Bäckman 2004; Boccalon 2000; Chong 2005; Koopman 1996; Levine 1996; Ramacciotti 2004), but adequate in a single trial (Daskalopoulos 2005) as it reported using a computerised process.

Allocation was adequately concealed in four trials (Bäckman 2004; Boccalon 2000; Koopman 1996; Levine 1996). Daskalopoulos 2005 did not report their method and allocation concealment was not reported in Chong 2005, so both were rated as unclear risk. In the Ramacciotti 2004 study, randomisation was reportedly done by blocks in an 'open manner', which we rated as high risk of bias.

Blinding (performance bias and detection bias)

Blinding refers to whether participants and study personnel knew which patients were in hospital and which received treatment at home. By the nature of this study blinding was never going to be easy to achieve. Five studies were open, non-blinded studies (Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004) and were judged to be of high risk of bias. Participants in Bäckman 2004 were allowed to change their assigned treatment or leave study after randomisation but we determined the risk of performance bias as low for the outcomes of this study. Although in Boccalon 2000 no blinding of participant or personnel was reported, both groups received the same treatment. All participants received an oral anticoagulant for the first three days. The review authors deemed the outcomes were unlikely to have been affected by lack of blinding of participants or personnel and so was at low risk of bias.

Four studies had independent outcome assessors and were deemed low risk of detection bias (Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996). In three studies blinding of outcome assessors was not reported and therefore deemed at high risk of detection bias (Bäckman 2004; Boccalon 2000; Ramacciotti 2004).

Incomplete outcome data (attrition bias)

Five of the seven included studies either reported on all participants or adequately described their loss-to-follow up and were rated as low risk (Bäckman 2004; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996). Ramacciotti 2004 and Boccalon 2000 had a high rate of attrition and were rated as high risk.

Selective reporting (reporting bias)

We assessed a study as being free of the risk of selective outcome reporting if both the following applied:

- the published report included all expected outcomes;
- outcomes were reported systematically for all comparison groups, based on prospectively collected data.

We deemed the risk of bias low if both of the criteria were met, unclear if these criteria were not met and high if there was

evidence that data had been collected on outcomes of interest but were not reported in the study publication.

We did not find any indication suggesting that the outcomes were selectively reported in the included studies so all studies were rated as low risk.

Other potential sources of bias

We had no concerns regarding other potential sources of bias for two studies (Boccalon 2000; Daskalopoulos 2005). For Bäckman 2004, Chong 2005, Koopman 1996, Levine 1996 and Ramacciotti 2004 there was insufficient information to judge whether there was a potential for other bias, so these were rated as unclear risk as each study had a large number of patients in the LMWH/home treatment group treated in hospital. Koopman 1996, Levine 1996 and Ramacciotti 2004 differed methodologically as participants randomised to LMWH were only treated at home as determined by a clinician, and not specifically assigned to home treatment. These studies were evaluated using sensitivity analysis for their impact on evidence produced through meta-analysis. These issues are further discussed in Overall completeness and applicability of evidence.

Effects of interventions

A summary of the findings of this review are presented in Summary of findings table 1. The outcomes of the included trials are summarised in Table 1.

Recurrent VTE (PE or recurrence of DVT)

Six studies reported on this outcome (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). The outcome follow-up time ranged from three months to one year. The pooled results showed a reduced recurrence of VTE between home and hospital treatment, with home treatment carrying less risk of recurrent VTE (RR 0.58, 95% CI 0.39 to 0.86; participants = 1708; studies = 6; I^2 = 0%; P = 0.007) (Analysis 1.1). The evidence was rated as low quality due to risk of bias and indirectness concerns.

Venous gangrene

There were no reports of venous gangrene in any of the included studies.

Heparin complications including major and minor bleeding

Six studies reported on this outcome (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). Follow-up of the outcome ranged from 14 days to one year.

On pooling the results of major bleeding, no differences between the home and hospital treatment groups on major bleeding were seen (RR 0.67, 95% CI 0.33 to 1.36; participants = 1708; studies = 6; I^2 = 0%; P = 0.27) (Analysis 1.2). The evidence was rated as low quality due to risk of bias and indirectness concerns.

For the outcome of minor bleeding no differences between the hospital and home treated arms on minor bleeding were seen (RR 1.29, 95% CI 0.94 to 1.78; participants = 1708; studies = 6; I^2 = 0%; P = 0.11) (Analysis 1.3). The evidence was rated as low quality due to risk of bias and indirectness concerns.

Death

Six studies included reports on death, with follow up ranging from three months to one year (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). A meta-analysis of the results did not show a difference in the numbers of deaths between the home and hospital treated groups (RR 0.69, 95% CI 0.44 to 1.09; participants = 1708; studies = 6; I^2 = 0%; P = 0.11) (Analysis 1.4). The evidence was rated as low quality due to risk of bias and indirectness concerns.

Patient satisfaction and Quality of Life

Three studies included data on quality of life (QoL), (Bäckman 2004; Koopman 1996; Levine 1996). Bäckman 2004 assessed QoL using the EuroQual tool EQ-5D and found no difference in the mean QoL scores or in the proportion of patients showing improvement in self-rated health state between the treatment groups. QoL was assessed immediately after treatment and after three months. A substantial number of patients randomised to in-patient care in this study chose out-patient treatment for the predominant reason of personal/social preferences. In the Koopman 1996 trial, QoL was measured using the Medical Outcome Study Short-Form 20 for a generic measure of physical and mental health, as well as adapted version of the Rotterdam Symptom Checklist, which is specific to thrombosis, and measures were taken at baseline, end of treatment course, as well as 12 weeks and 24 weeks after treatment. At 24 weeks after treatment over 80% of both trial groups had completed the QoL questionnaires. Overall, participants showed an improvement in QoL in both groups but two out of six criteria (physical activity and social functioning) showed an advantage in those in the LMWH group at the completion of initial treatment, but this difference was not seen at 12 or 24 weeks after treatment. The Levine 1996 study reported on QoL seven days after treatment using the Medical Outcomes Study Short-Form 36 (SF-36) which reports on eight physical and mental health domains. Only the social functioning domain showed a greater improvement in patients treated at home compared with heparin treatment, but there was no difference in the other domains between the two treatment groups (O'Brien 1999). We could not carry out meta-analysis for this outcome due to heterogeneity in reporting of QoL, as well as paucity of data reported by the studies.

The quality of evidence for this outcome was rated as very low due to risk of bias, indirectness and heterogeneity of measurement and reporting.

Cost effectiveness of treatment

Bäckman 2004, Boccalon 2000, Daskalopoulos 2005 and Koopman 1996 all reported on cost effectiveness of the treatment comparisons but due to the way the data were presented by the studies no meta-analysis could be performed for this outcome.

In the Bäckman 2004 study, which reported on costs within three months of treatment, 224 participants were eligible, 131 entered the trial and 124 completed the economic part of the study. Total direct costs were higher for those in the in-patient strategy group, i.e. Swedish Crown (SEK) 16,400 per patient (Euro 1899) compared to SEK 12,100 per patient (Euro 1405) in the out-patient (home) strategy group (P < 0.0010).

The Koopman 1996 trial followed participants for six months and the results were used for comparison of the cost of treatment calculations between the two arms of the trial (van den Belt 1998). There was a 64% saving in those treated with LMWH as opposed to UFH, largely due to lower hospital costs. The trialists stated that this was a conservative estimate of the potential reduction in costs. Similarly, an evaluation of those participants entered into the Levine 1996 trial (O'Brien 1999), showed a cost saving of 57%, and followed participants for three months. This latter figure is confirmed by Boccalon 2000 who showed that the mean cost of in-patient treatment over 10 days was more than 55% more expensive compared to the mean cost of outpatients over the same time period. Similarly, in Daskalopoulos 2005, which reported on 12 months of follow-up, estimated cost was slightly in favour of the LMWH group due to the significant cut in hospitalisation.

The quality of evidence for this outcome was rated as very low due to risk of bias, indirectness and heterogeneity of measurement and reporting.

Other outcomes of interest

None of the trials considered the incidence of post-thrombotic syndrome.

Mean hospital stay for patients without events such as bleeding or (suspected) recurrences in Koopman 1996 was 8.1 days for the hospital-treated 'control' group and 2.7 days for the home-treated 'treatment' group. In the other large trial (Levine 1996), the mean hospital stay was 6.5 days for the hospital-treated control group and 2.1 days for the home-treated group. Mean hospital stay in the Boccalon 2000 was 9.6 days for the hospital-treated group and one day for the home-treated group. The Ramacciotti 2004 trial had a mean hospital stay of three days for home-treated patients and seven days for the hospital-treated patients. Three studies did not report duration of hospital stay (Bäckman 2004; Chong 2005; Daskalopoulos 2005).

Thirty-six per cent of participants in the Koopman 1996 trial were treated entirely at home, 39% had a short hospital stay and 25% were entirely hospital treated. Fifty per cent of participants in the Levine 1996 trial were treated entirely at home. In the Daskalopoulos 2005 trial, no patient allocated to receive treatment with LMWH underwent any hospitalisation.

Seventy-seven percent of participants in the home arm (LMWH group) of the Chong 2005 trial were admitted to hospital. Twelve percent were released on the day of admission, 34% were kept for one day and 31% were kept for two or more nights. The Ramacciotti 2004 trial reported hospitalisation for all hospital-treated patients and 64% of home-treated patients.

Heterogeneity, subgroup analysis and sensitivity analysis

We found the heterogeneity in the pooled effect estimates to be very low and did not have reason to further investigate. When we performed sensitivity analysis we found no difference in the evidence when the studies with high risk of bias were removed (Ramacciotti 2004). There were no analyses that had a majority weight by a single study, so no sensitivity analyses was performed on these criteria. Sensitivity analysis was performed by evaluating the impact of the Koopman 1996 Levine 1996 and Ramacciotti 2004 trials due to the issue that participants randomised to LMWH were only treated at home as determined by a clinician, and not specifically assigned to home treatment. This sensitivity analysis did not change the findings of the meta-analyses.

Discussion

Summary of main results

This review presents low-quality evidence that patients treated at home with LMWH are less likely to have recurrence of VTE, compared to those treated in an in-patient (hospital) setting. No differences in major or minor bleeding events or mortality were seen (all low-quality evidence), indicating that home treatment is no worse for these outcomes when compared with in-patient treatment.

Overall completeness and applicability of evidence

While the results of this review are promising there are several concerns with the applicability of the evidence. Primarily, a large number of the participants in the home treatment group were not solely treated at home. Also, the treatment comparison was not always superior in the larger trials, and finally, there were a large number of eligible participants excluded prior to randomisation, raising concerns with applicability.

Many of the participants randomised to home treatment with a LMWH were not actually treated fully at home but hospitalised for some or all of the treatment period (See Table 2 for more details). Only 40% (Bäckman 2004), 23% (Chong 2005), 36% (Koopman 1996) 48.5% (Levine 1996) and 36% (Ramacciotti 2004), of those randomised to home treatment were treated wholly at home, and this makes the trials' results difficult to interpret. For three trials the participants that were randomised to the LMWH treatment, as opposed to the UFH, could be treated at home or in an in-patient setting at the discretion of the clinicians or investigators (Koopman 1996; Levine 1996; Ramacciotti 2004). This creates the concern that the data collected and reported in the meta-analyses may not directly speak to the question at hand. In order to

address these issues we conducted extensive sensitivity analyses and found there was no difference in our findings when the findings of these studies were excluded. This issue is not just a problem with these few trials but an overall, and possibly insurmountable one, as the nature of DVT and its complications may require in-patient treatment, even if a person is deemed acceptable for home treatment. However, these trials have shown that patients treated at home with LMWH are less likely to have recurrence of VTE compared to their counterparts treated in the hospital with UFH or LMWH. Also, participants were found to have preferred treatment at home. These concerns would most likely lead to a dilution of the conclusions of the review.

In the three major RCTs (Chong 2005; Koopman 1996; Levine 1996), UFH in hospital was compared with LMWH at home. A more methodologically sound trial would have compared LMWH in both groups and would have been justified by the many trials and three meta-analyses (Erkens 2010; Leizorovicz 1994; Lensing 1995) showing that LMWH is at least as effective as UFH.

Another factor limiting the conclusions of the review was the very high pre-randomisation exclusion rate reported by several of the trials (Boccalon 2000; Koopman 1996; Levine 1996). Koopman 1996 reported an exclusion of 31% of eligible participants and Levine 1996 reported 67%. Similarly, high exclusion rates were reported by Boccalon 2000 (78%), and Bäckman 2004 (42%). The exclusion criteria were very diffuse and could have been less strict. Daskalopoulos 2005 presented a contrasting low exclusion rate (7%). Ramacciotti 2004 and Chong 2005 did not report on pre-randomisation exclusions, except for three participants in the Chong 2005 trial who were enrolled but not randomised because they did not receive the study treatment or did not provide treatment-related data.

Although we have included 'economic analysis' as an outcome, a comprehensive economic analysis is beyond the scope/expertise of this review, so we have reported only on limited data available from the included studies.

Other issues that may affect applicability of our review are the limited number of participants from developing countries and the fact that no high-quality randomised control trials have been published after 2005.

Trends in the treatment of VTE have been changing recently with practitioners moving away from UFH and using more LMWHs and the newer class of direct oral anticoagulants (DOACs). Treatment with LMWHs and DOACs have been shown to be efficacious with no increase in clinically relevant complications (Robertson 2015; Robertson 2017). While UFH treatment is not going to disappear completely, due to its monitoring requirements and subsequent costs there has been a trend in practitioners moving away from its usage and embracing LMWH and DOACs. With DOACs, however, clinicians treating VTE have to reckon with their complexity, which include appropriate dose selection for the relevant indication, avoidance of drug-drug and drug-disease interactions, and consideration of dose adjustments in specific clinical situations, such as organ dysfunction (Finks 2016). This review did not evaluate any studies that included the use of DOACs, such as rivaroxaban or dabigatran, as no such studies met our inclusion criteria. We therefore have limited evidence from this review to discuss their use in detail.

Quality of the evidence

Strengths of the evidence include the consistency and homogeneity of the results from the individual studies as well as the sufficient number of participants and events included for each outcome. However, the evidence generated in the review was downgraded to low quality due to concerns with risk of bias of the individually included studies as well as with indirectness of the data due to the issues of participants randomised to home treatment being hospitalised, as discussed in the above section. A major concern with risk of bias was selection bias: all seven included studies were at unclear or high risk for either concerns with random sequence generation or allocation concealment. Although minimising performance bias would be very difficult due to the open nature of the treatment, making blinding of the participants and personnel nearly impossible, these issues could be addressed in other ways such as keeping the treatment drugs consistent between interventions or also demonstrating more stringent control of detection bias. Risk of bias concerns led us to downgrade the evidence by one level. These concerns reduce the robustness of the findings. See Summary of findings table 1 for further information.

Sensitivity analysis was conducted by evaluating the strength of the evidence in light of the risk of bias issues as well concerns with indirectness, and we found that the findings did not change when studies with high risk of bias, or studies that may not have directly contributed to the objective of the review, were removed.

Publication bias was not investigated for the review because less than 10 studies were included in the individual meta-analyses. Less than 10 studies will not produce robust results in the funnel plots used to investigate publication bias.

Potential biases in the review process

All possible measures to reduce potential biases were adhered to during the review process, including conducting a comprehensive search, double data extraction and grading of the evidence. All attempts were made to identify relevant studies and disagreements were discussed thoroughly.

Agreements and disagreements with other studies or reviews

The results of uncontrolled trials encompass a considerable body of evidence (Table 3), particularly in relation to practical questions (see Implications for research). An observational study that included 334 patients concluded that community-based treatment of thromboembolism was safe and effective (Hyers 2007). Home treatment has also been investigated in specific pathological communities including cancer patients, and found to be a suitable alternative to in-patient care (Ageno 2005).

In the UK, some local health authorities (Trusts) have published the results of uncontrolled studies. Swindon Trust reported 373 patients referred to the program of whom 32% had proven DVT and 37.5% were treated wholly or

partially at home (Green 1998). Chertsey Trust reported on 1093 referrals of which 160 were proven to have DVT. All but one i.e. 159 patients, were home-treated (O'Shaugnessy 1998). There were no complications apart from two minor bleeds. The savings to the Chertsey Trust was estimated as £320,000 over 22 months. In a combined presentation to the American Thoracic Society, three trusts reported managing 966 patients with DVT of whom only 10% were admitted to hospital (Miles 1998). In Norwich, 447 patients were referred over a six-month period, scans were positive in 30% and, of these, 20% were considered unsuitable for home treatment (Wimperis 1998). Thus, 105 were treated and five had to be re-admitted - two with suspected PE (scans negative), one with PE, one with stroke, and one with an unrelated illness.

A study from Melbourne (Ting 1998), presented 100 patients with proven DVT. Fifty-three patients had proximal thrombosis and were admitted for one day for investigation, including lung scan: 16 scans were positive although the patients were asymptomatic and the result did not affect their management at home. The 47 patients with distal thrombosis were treated entirely at home. There was initial extension of clot in 13.2% of distal and 2.7% of proximal thromboses but at follow-up scans at six months, 60.7% of distal and 18.5% of proximal thromboses had completely resolved. The only complications were six minor bleeds. The numbers of patients referred but cleared of DVT, and the numbers rejected by the protocol were not mentioned. In a Swedish study (Lindmarker 1996), 434 patients with DVT were treated in hospital for three days before discharge home on treatment. Three patients had proven PE: there was one major bleed and 16 minor ones. There were no deaths in the acute stage and no extension of thromboses. In Grau 1998, 39 out of 71 patients with DVT were treated at home. There was no instance of PE and only one minor bleed. These trials all reported worthwhile cost savings. Only one uncontrolled study reported on patient satisfaction (Conner 1999). Seventy-nine per cent were happy to be treated at home, 12% would have preferred hospital and nine per cent had no preference.

Although not based on evidence from randomised controlled trials, cost savings in favour of home treatment have been shown wherever calculated. Hospital Episode Statistics for the UK for 1993 (Griffin 1996), show 17,000 admissions for PE and 25,000 for DVT with an average in-patient stay of 7.2 days. At an estimated cost of £200 per in-patient day (1998 figures), hospitalisation costs alone amount to £60,480,000. If this could be reduced to, say, two days in 75% of cases at a cost of £12,600,000, a saving of £47,880,000 on bed costs per annum is realisable. Although it was not in the remit of this review, it is worth noting that surveillance of participants up to four years after randomisation to home or hospital regimens showed no difference between the groups (Grau 2001).

Regarding the results of quality of life outcomes reported in Bäckman 2004, a similar preference was observed in two thirds of patients in Blattler 1998, (excluded from our review as it was not an RCT), who challenged hospital confinement and stated that they would not choose hospitalisation another time. The Blattler trial also reported that their home treatment group was free of symptoms a day earlier and returned to work a week earlier than the hospital group (Blattler 1998).

Authors' conclusions

Implications for practice

This review presents low-quality evidence that patients treated at home with LMWH are less likely to have recurrence of VTE compared to those treated in hospital. No clear differences in major or minor bleeding complications, or mortality were seen (low-quality evidence), indicating treatment at home with LMWHs is not more harmful than treatment in an in-patient setting with LMWHs or UFHs. Despite the limitations in the reviewed trials, there is low-quality evidence to suggest that home treatment of DVT is more effective than standard hospital treatment.

Implications for research

It is unlikely that definitive evidence of the safety of home treatment will be forthcoming for reasons addressed in the discussion. This is underscored by the fact that no further high-quality randomised control trials published after 2005 have been identified in our search. Also, treatment of thromboembolism with LMWHs is being incorporated into local health authority guidelines that include at home administration practices (East Lancashire Health Economy 2015; Wong 2014). Further information will consist of accumulation of a larger database of uncontrolled studies that can only be compared with historical controls. There may be anecdotal notes of failure but, as these will be rare, it is possible they will not be published.

It has been suggested by Baron 1999 that patients should be allocated on a triage basis: (1) standard in-patient regimen for those with intercurrent illness or massive VTE; (2) partial home treatment for those diagnosed in hospital but fit enough for discharge; and (3) those treated completely at home. The ideal trial would compare LMWH only in each arm, would exclude 25% or fewer participants from entry into the trial, and would present the results in three groups. These issues should be given further examination.

Some practical issues remain to be resolved.

- Should the patient be admitted at all if suitable for home treatment?
- Should LMWH be given on suspicion or only on confirmation of the diagnosis?
- How would the treatment comparison alter using newer direct oral anticoagulants compared with more traditional LMWH?
- Should exclusion criteria be relaxed to favour greater entry to home treatment? For example, should a healthy pregnancy preclude home treatment?
- Should a screening test such as D-dimer levels be used?
- Should the system be controlled by the traditional physician's team or should specialist anticoagulant nurses be trained

and, if so, will there still be a lead clinician to accept overall responsibility?
- Development of local guidelines which contain clinical prediction rules, biomarkers and imaging which can be used to tailor therapy to the severity of the disease.
- Training community healthcare workers to administer and monitor treatment progress.

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Contributions of authors

EO: independently selected the articles, assessed studies for inclusion and assessed the methodological quality of selected trials, extracted data, data entry, analysis and drafted the report, evaluated the evidence of the review, contributed to the discussion of the final report of the review
RO: independently selected the articles, assessed studies for inclusion and assessed the methodological quality of selected trials, extracted data, and contributed to the discussion of the final report of the review
RF: data entry, analysis and drafted the report, evaluated the evidence of the review, contributed to the discussion of the final report of the review

Declarations of interest

RO: none known
EO: none known
RF: none known

Differences between protocol and review

The methodological quality of the included studies is assessed using Cochrane's Risk of bias tool (Higgins 2011) instead of the previously used method by Jadad 1996. We have added a summary of findings table and assessed the quality of the evidence according to GRADE (Atkins 2004).

The secondary outcome of patient satisfaction was broadened to include quality of life as this outcome is becoming more commonly used and is well accepted.

Outcomes 'PE' and 'recurrent DVT' renamed as 'Recurrence of VTE'.

Published notes

Characteristics of studies

Characteristics of included studies

Boccalon 2000

Methods	Study design: randomised controlled trial Exclusions post-randomisation: one patient withdrew consent following randomisation, 7 patients withdrew due to severe complications (3 DVT extensions, 4 major haemorrhages) Losses to follow up: 38 participants did not complete the 6 months follow up (with those being treated in hospital twice as likely to withdraw) Intention to treat analysis: not indicated
Participants	Country: France Setting: home or hospital N: 204 randomised, 201 included (102 hospital, 99 home) representing 11.8% of those eligible Age: mean 63.8 ± 14.1 years, range 18 to 85 years Sex: 113 males: 88 females Inclusion criteria: confirmed diagnosis (by ultrasonography or venography) of proximal DVT not more than 30 days before enrolment Exclusion criteria: thrombus in the inferior vena cava, a floating thrombus, history of DVT within the previous 6 months, DVT with symptomatic PE, a clinical condition requiring hospitalisation, contraindication to anticoagulant treatment, pregnancy, heparin treatment within the 48 hours preceding inclusion, home or hospital treatment were impossible for any reason, participant lived too far away from the trial centre, written consent was not given Participants were also examined, though not necessarily excluded, for risk factors for DVT, including previous thromboembolism, varicose veins, immobilization, surgery, trauma, cancer, use of oral contraceptive, known or inherited clotting disorders, other co-morbidities such as cardiovascular disease with right ventricular failure
Interventions	Treatment: sc injection of LMWH (dalteparin sodium, enoxaparin sodium or nadroparin calcium as chosen by the attending physician) at the recommended dose followed by anticoagulant for 6 months at home Control: sc injection of LMWH (dalteparin sodium, enoxaparin sodium or nadroparin calcium as chosen by attending physician) at the recommended dose followed by anticoagulant for 6 months initially in hospital for 10 ± 2 days then at home Anticoagulants: oral VKA or fluindione, 20 mg/day for the first 3 days, followed by regimen to maintain INR between 2.0 and 3.0 for up to 6 months Participants were also given compression stockings and were encouraged to return to physical activity according to a schedule approved by the general practitioner and nurse
Outcomes	Primary: recurrent VTE, PE, major bleeding Secondary: death, minor bleeding, economic analysis Duration of follow-up: six months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias)	Low risk	Although no blinding of participant or personnel was reported both groups received the same treatment. All patients received an oral anticoagulant for the first 3 days. Outcome is unlikely to have been affected by lack of blinding of participants or personnel
Blinding of outcome assessment (detection bias)	High risk	Blinding of outcome assessors not reported. Outcome could have been influenced by lack of blinding
Incomplete outcome data (attrition bias)	High risk	38 participants did not complete the 6 months follow up (with those being treated in hospital twice as likely to withdraw)
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	Low risk	No other potential bias identified

Bäckman 2004

Methods	Study design: randomised multicentre trial Exclusions post-randomisation: 7 patients excluded (5 randomised to inpatient treatment refused to cooperate, and 2 randomised to outpatient/home treatment had a drug reaction and haematuria, respectively Losses to follow-up: none Intention to treat analysis: yes
Participants	Country: Sweden Setting: inpatient or outpatient/home N: 224 met inclusion criteria, 131 randomised (66 inpatient, 65 outpatient/home) representing 58% of those eligible Age: mean 66 (33 - 87) years, inpatient group; 67 (25 - 91) years, outpatient/home group Sex: male/female ratio, 34/34 inpatient group; 34/31 outpatient group Inclusion criteria: acute symptomatic DVT confirmed by phlebography or ultrasound in patients aged 18 years and older presenting at the emergency department Exclusion criteria: not clearly stated
Interventions	All patients were provided with intervention stockings. Both groups were treated with LMWH administered sc once daily, adjusted for body weight, for at least 5 days until prothrombin time was < 25% (INR > 2.0) for at least 1 day Outpatient/home: treatment included a daily visit to the outpatient department at a primary care centre or else a visit by the district nurse at the patient's home, depending on the local circumstances or patient preference Inpatient: patients were admitted to the ward
Outcomes	Direct medical and direct non-medical costs Duration of follow-up three months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The method used to generate the random sequence is not described by the authors
Allocation concealment (selection bias)	Low risk	Randomisation was performed centrally by means of codes in envelopes in batches of 20 in accordance with Zelen 1979
Blinding of participants and personnel (performance bias)	Low risk	Although participants were allowed to change their assigned treatment or leave study after randomisation, the review authors determined the risk of performance bias as low
Blinding of outcome assessment (detection bias)	High risk	Not described; outcomes could have been influenced by lack of blinding
Incomplete outcome data (attrition bias)	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Pre-specified outcomes included
Other bias	Unclear risk	Insufficient information to determine if other potential bias exist; only 40% of participants randomised to treatment with LMWH were actually treated at home

Chong 2005

Methods	Study design: randomised parallel-group open study Exclusions post-randomisation: 63 (20%) were not included in the primary outcome analysis Losses to follow-up: 45 had no analysis at 24 weeks Intention-to-treat analysis: yes
Participants	Countries: Australia, New Zealand, Poland, South Africa Setting: outpatient or hospital N: 301 enrolled; 298 randomised (148 hospital, 150 home) Age: 18+ years Sex: 156 males, 142 females Inclusion criteria: diagnosis of symptomatic lower extremity DVT (proximal or distal) confirmed by either contrast venography and/or ultrasonography, be suitable for treatment in an outpatient setting, be prepared to self administer daily sc injections, life expectancy > 6 months Exclusion criteria: 1) received therapeutic doses of heparin for more than 24 hours before randomisation; 2) clinically overt signs or symptoms of PE or evidence of PE on lung scanning or pulmonary angiography; 3) impending venous gangrene; 4) previous HIT or another hypersensitivity reaction to heparin; 5) a platelet count < 50 x $10/^{9}$ per litre; treatment with fibrinolytics or oral anticoagulants within the previous 5 days, or with other investigational therapeutic agents within the previous 4 weeks; 6) pregnancy or lactation; 7) any clinical significant medical condition other than DVT that would prevent the patient from being discharged from hospital
Interventions	Treatment: once daily sc injection of LMWH enoxaparin 1.5 mg/kg for a minimum of 5 days plus 10 mg of warfarin for 3 months with dose adjusted to achieve and maintain the INR above 2 and within range accepted by the investigator Control: 5000 IU bolus of UFH for a minimum of 5 days plus 10 mg warfarin started on day 1 of the treatment for 3 months
Outcomes	Primary: efficacy endpoint: incidence of symptomatic recurrent DVT Safety endpoint: incidence of adverse effect, major or minor bleeding during the first 14 days Secondary: incidence of PE, recurrent VTE Duration of follow up: 24 weeks
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Did not report use of adequate random sequence generation
Allocation concealment (selection bias)	Unclear risk	Did not report use of adequate concealment technique
Blinding of participants and personnel (performance bias)	High risk	Treatment was not blinded
Blinding of outcome assessment (detection bias)	Low risk	Assessors were independent of the study and investigators and unaware of the treatments that patients were receiving
Incomplete outcome data (attrition bias)	Low risk	All outcome data reported
Selective reporting (reporting bias)	Low risk	All pre-specified primary and secondary safety endpoints were reported
Other bias	Unclear risk	Insufficient information to determine if other potential bias exist; only 23% of participants randomised to treatment with LMWH were actually treated exclusively at home

Daskalopoulos 2005

Methods	Study design: prospective randomised trial Exclusions post randomisation: 6 patients withdrew consent following randomisation Losses to follow-up: none Intention to treat analysis: yes
Participants	Country: Greece Setting: outpatient or hospital N: 108 randomised (55 LMWH, 53 UFH) Age: 18 years and over, range 23 to 95, mean 58.6 years Sex: 61 female, 41 male Inclusion criteria: acute proximal DVT confirmed by colour duplex ultrasound scan not more than 1 week onset Exclusion criteria: segmental DVT restricted to infrapopliteal deep veins or calf muscles as determined by duplex ultrasonography, symptomatic or clinically suspected PE, history of recently diagnosed (within 12 months) DVT or PE, patient already on anticoagulant therapy, bleeding tendency objectively confirmed, hypersensitivity to heparin preparations or coumarin derivatives, uncontrolled hypertension, history of recently diagnosed (less than 1 month) cerebrovascular accident, intracranial artery aneurysm, infectious endocarditis, thrombocytopenia, active peptic ulcer, hepatic or renal failure, history of asthma, recent spinal or epidural anaesthesia or intraspinal paracentesis (less than 5 days), recent surgery (less than 5 days), recently performed thrombolysis or under antiplatelet therapy, body weight less than 35 kg, pregnancy, illicit drug addiction, altered mental status or impaired cognitive function with inability to comply with study protocol
Interventions	Treatment: single sc injection of LMWH (tinzaparin sodium) in a weight adjusted dose (175 anti Xa IU/Kg) daily for 6 months Control: iv bolus of 5000 IU UFH followed by iv infusion of UFH for 5 to 7 days. APTT was measured after 4 hours of the initiation of heparin administration and was repeated 6 hours thereafter to reach the therapeutic range (ratio: 1.5 to 2.5) Oral anticoagulant was commenced on the 3rd day following UFH therapy
Outcomes	Primary: recanalisation of the thrombosed veins, major events Secondary: recurrent DVT, PE, major bleeding, minor bleeding, thrombocytopenia, death Duration of follow-up: 12 months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was by means of a computer schedule
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias)	High risk	The study was open-label
Blinding of outcome assessment (detection bias)	Low risk	Because a double blind study was not feasible, all objective diagnostic tests were interpreted by specialists including Coagulation Unit staff and radiology staff who were not involved in the study
Incomplete outcome data (attrition bias)	Low risk	All outcome data were reported
Selective reporting (reporting bias)	Low risk	All pre-defined endpoints data were reported
Other bias	Low risk	No other potential bias was identified

Koopman 1996

Methods	Study design: randomised controlled trial Exclusions post- randomisation: two (both withdrew consent, one from each group) Losses to follow up: two patients in each group were lost to follow up at 12 weeks Intention to treat analysis: yes
Participants	Countries: The Netherlands, France, Italy, New Zealand, Australia Setting: home or hospital N: 400 randomised (202 LMWH, 198 UFH) Age: 59 ± 17 years LMWH group, 62 ± 16 years UFH group Sex: 203 males: 197 females Inclusion criteria: acute symptomatic proximal DVT proven by venography or duplex scan Exclusion criteria: VTE within previous 2 years, suspected PE at presentation, geographic inaccessibility, PTS, less than 18 years old, pregnancy, life expectancy less than 6 months, previous treatment with heparin for more than 24 hours
Interventions	Treatment: twice daily injections of LMWH (nadroparin calcium (Fraxiparine) at a dose adjusted for patient's weight) at home when appropriate; Patients were instructed by nurse on how to administer the injections themselves Control: UFH (APTT adjusted dose, continuous iv infusion of 1250 IU per hour after initial iv bolus of 5000 IU) in hospital Duration: minimum 5 days, maximum 24 weeks Oral anticoagulation: warfarin commenced on day 1 and continued for 3 months, dose adjusted to give INR 2.0 to 3.0
Outcomes	Primary: Symptomatic recurrent VTE Secondary: major haemorrhage, death, quality of life comparisons, comparison of costs (in-patient versus home) Duration of follow-up: six months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	Allocation was by means of a central 24-hour telephone service
Blinding of participants and personnel (performance bias)	High risk	Unblinded trial
Blinding of outcome assessment (detection bias)	Low risk	Objective testing was done blindly as well as documentation of all potential outcome events were assessed by an independent adjudication committee whose members were unaware of the treatment assignments
Incomplete outcome data (attrition bias)	Low risk	All losses to follow up were reported
Selective reporting (reporting bias)	Low risk	All pre-specified outcome measures were reported
Other bias	Unclear risk	Insufficient information to determine if other potential bias exist; only 36% of participants randomised to treatment with LMWH were actually treated at home

Levine 1996

Methods	Study design: randomised controlled trial Exclusions post-randomisation: not stated Losses to follow up: none Intention to treat analysis: not indicated but analysis included all randomised participants
Participants	Country: Canada Setting: home or hospital N: 500 randomised (247 LMWH, 253 UFH) Age: mean 57 ± 17 years LMWH group, 59 ± 15 years UFH group Sex: 301 males: 199 females Inclusion criteria: acute proximal DVT proven on venography or duplex scan Exclusion criteria: two or more previous episodes of DVT or PE, active bleeding, active peptic ulcer, coagulation disorder, symptomatic PE, possibility of non-compliance, contraindications to LMWH, pregnancy, pre-treatment with heparin for more than 48 hours, inability to make follow up visits due to geographical inaccessibility, presence of known deficiency of anti-thrombin III, protein C or protein S
Interventions	Treatment: sc LMWH (enoxaparin 1 mg per kg body weight twice a day) primarily at home Control: UFH (APTT adjusted dose, continuous iv infusion of 20,000 IU after initial iv bolus of 5000 IU) in hospital Duration: minimum 5 days Anticoagulants: warfarin sodium started on evening of day 2 and continued for at least 3 months. First dose 10 mg, thereafter adjusted to maintain INR between 2.0 and 3.0
Outcomes	Primary: symptomatic recurrent DVT or PE within 90 days of randomisation, major bleeding, minor bleeding during study period and up to 48 hours after discontinuation of study medication Secondary: death, economic evaluation Duration of follow-up: three months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	Assignment of treatment was over the telephone from a central site
Blinding of participants and personnel (performance bias)	High risk	Unblinded
Blinding of outcome assessment (detection bias)	Low risk	Testing and assessment of recurrent VTE and bleeding were conducted by a committee unaware of the treatment assignments.
Incomplete outcome data (attrition bias)	Low risk	There were no losses to follow-up
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes were reported
Other bias	Unclear risk	Insufficient information to determine if other potential bias exist; only 48.5% of participants randomised to treatment with LMWH were actually treated at home

Ramacciotti 2004

Methods	Study design: randomised, open label, multicenter clinical trial Exclusions post-randomisation: not stated Losses to follow-up: 53.6% at 6 months of follow up Intention to treat analysis: not indicated but analysis included all randomised participants
Participants	Country: Brazil Setting: home or hospital N: 201 randomised (104 enoxaparin, 97 UFH) Age (years): mean 64 for home, 44 for hospitals Sex: 69 Males, 132 Females Inclusion criteria: age greater than or equal to 18 years, weight greater than or equal to 50 kg and < 110 kg, DVT symptoms for greater than or equal to 10 days, proximal lower limb DVT (confirmed by duplex ultrasound or venography), ready access to local health service, capable of using enoxaparin at home Exclusion criteria: history of HIT or allergy to heparin, haemorrhagic diathesis, surgery within 7 days, symptoms of PE, bilateral DVT, survival prognosis < 6 months, hepatic or renal failure, received therapeutic doses of UFH or LMWH for greater than or equal to 24 hrs in the previous 48 hrs, patients in hospital for another reason, with stay anticipated to last > 3 days, initial platelet count < 100,000/ml, uncontrolled hypertension with DBP greater than or equal to 180, initial APTT > 1.3 time the normal value, INR > 1.5 at enrolment, indication for thrombolysis or venous thrombectomy
Interventions	Treatment: once daily sc injection of LMWH enoxaparin at a dose of 1.5 mg/kg for 5 to 10 days given at home or in hospital at the discretion of the health care provider Control: iv bolus injection of 5000 IU of UFH followed by iv 500 IU/kg/day adjusted to maintain an APTT of 1.5 to 2.5 times the normal value for 5 to 10 days in hospital Anticoagulant: all patients received warfarin (with a targeted INR 2 to 3) for at least 3 months, starting at day 1 or 2 of treatment
Outcomes	Primary: recurrent DVT, PE Secondary: major and minor bleeding Duration of follow-up: six months
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was by block 1:1 at each centre to ensure balanced in each treatment arm but method of random sequence generation was not reported
Allocation concealment (selection bias)	High risk	Each investigator received the randomisation scheme specifying the treatment allocation for each patient enrolled in the study. Thus the investigator could foresee assignments and thus introduce selection bias
Blinding of participants and personnel (performance bias)	High risk	Open-label
Blinding of outcome assessment (detection bias)	High risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Only 32.7% of enoxaparin and 46.4% UFH patients were followed up after 6 months
Selective reporting (reporting bias)	Low risk	All pre-specified safety endpoints were reported
Other bias	Unclear risk	Insufficient information to determine if other potential bias exist; only 36% of participants randomised to treatment with enoxaparin were actually treated at home

Footnotes

APTT: activated partial thromboplastin time
DBP; diastolic blood pressure
DVT: deep vein thrombosis
HIT: heparin-induced thrombocytopenia
INR: international normalised ratio
IU: international units
iv: intravenous
LMWH: low molecular weight heparin
PE: pulmonary embolism
PTS: post-thrombotic syndrome
PTT: partial thromboplastin time
sc: subcutaneous
UFH: unfractionated heparin
VKA: vitamin K antagonist
VTE: venous thromboembolism

Characteristics of excluded studies

Aujesky 2011

Reason for exclusion	Assessed effectiveness, safety and efficacy of outpatient versus inpatient care for patient with acute PE and not DVT

Belcaro 1999

Reason for exclusion	Participants were randomised to different forms of heparin rather than to home or hospital treatment

Blattler 1998

Reason for exclusion	Although this study is published as an RCT the methodology does not meet the criteria for an RCT

Buller 2004

Reason for exclusion	Compared once daily LMWH with twice daily doses in the outpatient setting and not hospital versus home

Conner 1999

Reason for exclusion	Uncontrolled trial

Fitzmaurice 2000

Reason for exclusion	This study was concerned with the monitoring of oral anticoagulation at home or in the GP surgery

Frank 1998

Reason for exclusion	Although this study is published as an RCT the methodology does not meet the criteria for an RCT

Goldhaber 1998

Reason for exclusion	Participants randomised to home care with LMWH were first required to be treated in hospital before being discharged

Grau 1998

Reason for exclusion	Not a randomised trial

Grau 2001

Reason for exclusion	Retrospective study

Green 1998

Reason for exclusion	Uncontrolled trial

Hull 2000

Reason for exclusion	Trial concerned with prophylactic regimens using LMWH in patients undergoing hip arthroplasty

Hull 2002

Reason for exclusion	Trial concerned with evaluating two long term LMWH treatment protocols

Hull 2009

Reason for exclusion	Not home versus inpatient care, both groups of patients treated outside hospital. Usual care was defined as tinzaparin for five days or more followed by warfarin for 12 weeks

Lindmarker 1996

Reason for exclusion	Uncontrolled trial

Miles 1998

Reason for exclusion	Uncontrolled trial

Modesto-Alapont 2006

Reason for exclusion	Investigated the use of LMWH administered at home for the prevention of VTE in patients with severe chronic obstructive pulmonary disease

O'Shaugnessy 1998

Reason for exclusion	Uncontrolled trial

Otero 2010

Reason for exclusion	Focused on PE and not DVT

Pineo 2003

Reason for exclusion	Trial concerned with evaluating two long term LMWH treatment protocols

Rymes 2002

Reason for exclusion	Retrospective study

Ting 1998

Reason for exclusion	Uncontrolled trial

Wells 1998

Reason for exclusion	Controlled trial of nurse versus patient injection. Not related to admission or home treatment

White 1989

Reason for exclusion	This trial was concerned with the monitoring of oral anticoagulation at home or in the GP surgery

Wilson 2003

Reason for exclusion	Study design not home versus in-patient, anticoagulant clinics versus family physician clinic. Intervention was oral anticoagulant and not LMWH. The study population was anyone who required warfarin for at least three months and not specifically DVT

Wimperis 1998

Reason for exclusion	Uncontrolled trial

Footnotes

DVT: deep vein thrombosis
LMWH: low molecular weight heparin
PE: pulmonary embolism
RCT: randomised controlled trial
UFH: unfractionated heparin
VTE: venous thromboembolism

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

1 Treatment of DVT at home compared to treatment of DVT in hospital

How does treatment of DVT at home compared to treatment of DVT in hospital?

Patient or population: people with a diagnosed DVT
Setting: hospital and home
Intervention: treatment of DVT at home with LMWH[1]
Comparison: treatment of DVT in hospital with UFH or LMWH[2]

Outcomes	№ of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Comments
				Risk with treatment of DVT in hospital	Risk difference with Treatment of DVT at home	
Recurrence of VTE follow-up: range 3 months to 12 months	1708 (6 RCTs)	⊕⊕⊖⊖ LOW [3,4]	RR 0.58 (0.39 to 0.86)	Study population		
				74 per 1,000	31 fewer per 1,000 (45 fewer to 10 fewer)	
Venous gangrene	see comment					This outcome was not reported by any of the included studies
Major bleeding follow-up: range 14 days to 12 months	1708 (6 RCTs)	⊕⊕⊖⊖ LOW [3,4]	RR 0.67 (0.33 to 1.36)	Study population		
				21 per 1,000	7 fewer per 1,000 (14 fewer to 8 more)	
Minor bleeding follow-up: range 14 days to 12 months	1708 (6 RCTs)	⊕⊕⊖⊖ LOW[3,4]	RR 1.29 (0.94 to 1.78)	Study population		
				72 per 1,000	21 more per 1,000 (4 fewer to 56 more)	
Death follow-up: range 3 months to 12 months	1708 (6 RCTs)	⊕⊕⊖⊖ LOW[3,4]	RR 0.69 (0.44 to 1.09)	Study population		
				49 per 1,000	15 fewer per 1,000 (28 fewer to 4 more)	
Patient satisfaction/Quality of life follow-up: range 7 days to 6 months	1031 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[3,4,5]	-	See comment		Two studies reported greater improvements in QoL in patients treated at home compared with in-patient treatment, the third study reported a large number of participants chose to switch from in-patient care to home based care, suggesting it is the patient's preferred option
Cost effectiveness [6] follow up: range 10 days to 6 months	834 (4 RCTs)	⊕⊖⊖⊖ VERY LOW[3,4,5]	-	See comment		One study carried out a randomised economic evaluation and reported total direct costs were higher for those in the inpatient strategy group, i.e. Swedish Crown (SEK) 16,400 per patient (Euro 1,899) compared to SEK 12,100 per patient (Euro 1,405) in the outpatient (home) strategy group (P < 0.0010). This was supported by three other studies who reported on costs

*We calculated the assumed risk of the hospital treatment group from the average risk in the hospital treatment group (i.e. the number of participants with events divided by total number of participants of the hospital treatment group included in the meta-analysis). **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **DVT:** Deep vein thrombosis; **LMWH:** low molecular weight heparin, **RR:** Risk ratio; **UFH:** unfractionated heparin, **VTE:** Venous thromboembolism

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Footnotes

[1] Home treatment refers to treatment for DVT with a LMWH that occurs outside of a hospital or in-patient setting and can include the medication being administered by the participant or by a carer
[2] Hospital treatment refers to treatment for DVT with either a LMWH or UFH in a hospital or in-patient setting which is administered by care staff
[3] Downgraded one level due to risk of bias from unclear randomisation techniques and blinding measures in a majority of the included studies
[4] Downgraded one level due to indirectness because most of the included studies had a low number of participants actually treated at home with a LMWH and many were treated in hospital
[5] Downgraded one level due to heterogeneity because the included studies used different methods and time points in which to gather information of this outcome
[6] We are reporting on the cost effectiveness analysis reported in the included studies. We have not carried our an economic analysis ourselves

Additional tables

1 Summary of outcomes

Study	Setting	Number participants entered	Heparin type	Mean hospital stay (days)	Recurrence of VTE (%)	Major bleeding (%)	Minor bleeding (%)	Death (%)	Mean total direct costs per participant
Bäckman 2004									
	Hospital	65	LMWH	3.6	-	-	-	-	SEK 16,400
	Home	66	LMWH	1.6	-	-	-	-	SEK 12,100
Boccalon 2000									
	Hospital	102	LMWH	9.5	2.0	2.0	10.8	2.0	Fr 20,932
	Home	99	LMWH	1.4	1.0	2.0	17.2	0	Fr 9,230
Chong 2005									
	Hospital	148	UFH	-	9.5	2.0	11.5	1.4	-
	Home	150	LMWH	-	2.7	0	10.0	1.3	-
Daskalopoulos 2005									
	Hospital	53	UFH	-	11.3	7.5	5.7	3.8	-
	Home	55	LMWH	-	9.1	3.6	5.5	1.8	-
Koopman 1996									
	Hospital	198	UFH	8.1	8.6	2.0	7.6	8.1	-
	Home	202	LMWH	2.7	6.9	0.5	13.4	6.9	-
Levine 1996									
	Hospital	253	UFH	6.5	6.7	1.2	2.3	6.7	-
	Home	247	LMWH	2.1	5.3	2.0	2.4	4.5	-
Ramacciotti 2004									
	Hospital	97	LMWH	3	2	2	12	-	-
	Home	104	UFH	7	7	3	9	-	-

Footnotes

LMWH: low molecular weight heparin
UFH: unfractionated heparin
VTE: venous thromboembolism

2 Percentage of patients treated at home

Patients	Bäckman 2004	Boccalon 2000	Chong 2005	Daskalopoulos 2005	Koopman 1996	Levine 1996	Ramacciotti 2004
Randomised (N)	131	201	298	108	400	500	201
Excluded after randomisation (%)	5.3	18.9	20	5.5	0	0	0
Participants randomised to home/LMWH treat that were actually treated at home (not hospitalised) (%)	40*	74	23**	100***	36	48.5	36

Footnotes

*Bäckman 2004 reported 40% of those randomised to home treatment remained at home, and 40% were hospitalised; it is unclear what happened with the remaining 20%; 36 randomised participants changed treatment, 26 of whom changed from hospital to home and 10 from home to hospital

**Chong 2005 23% of those randomised to home treatment were exclusively treated at home, 12% were hospitalised and discharged within a day, 35% were hospitalised for one night, 23% for two nights and 8% for three or more nights

***Daskalopoulos 2005 initially reported "Patients allocated to receive treatment with LMWH underwent no hospitalizations at all", but later in the text they state "The number of major events requiring hospitalization was significantly lower in the LMWH group", making it unclear if those randomised to LMWH were exclusively treated at home

LMWH: low molecular weight heparin

3 Uncontrolled trials - patient demographics

Author	Referrals	Positive scans	% home treated
Grau 1998	-	71	55.0
Green 1998	373	119	37.5
Lindmarker 1996	-	434**	100.0
Miles 1998	-	966	90.0
O'Shaugnessy 1998	1093	160	99.9
Ting 1998	-	53*	100.0
Wimperis 1998	447	134	80.0
Total		1451	

Footnotes

* Excluding distal thrombosis
** 3 days hospital treatment before discharge

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Classification pending references

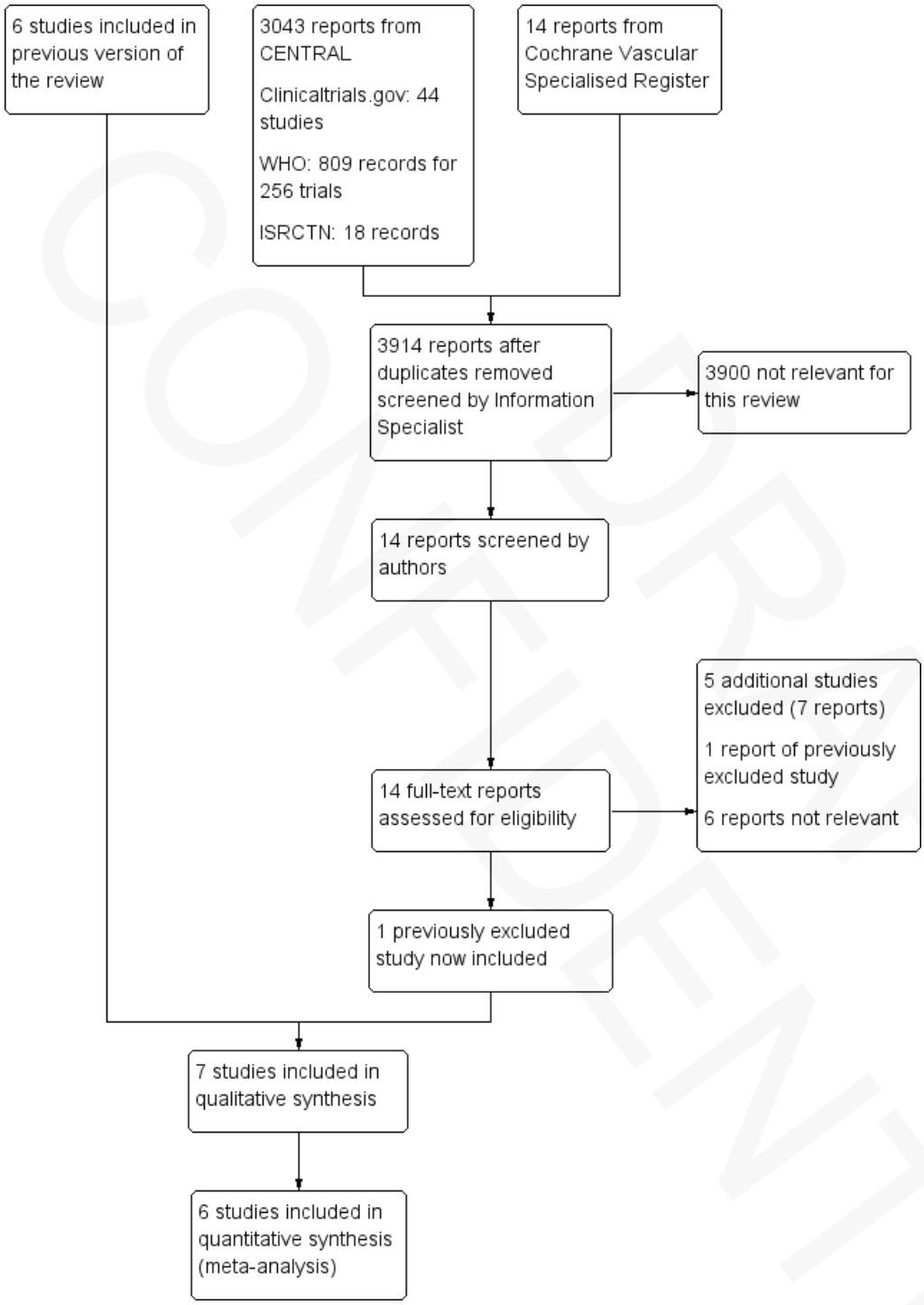
Data and analyses

1 Treatment of DVT at home versus treatment of DVT in hospital

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Recurrence of VTE	6	1708	Risk Ratio(M-H, Fixed, 95% CI)	0.58 [0.39, 0.86]
1.2 Major bleeding	6	1708	Risk Ratio(M-H, Fixed, 95% CI)	0.67 [0.33, 1.36]
1.3 Minor bleeding	6	1708	Risk Ratio(M-H, Fixed, 95% CI)	1.29 [0.94, 1.78]
1.4 Death	6	1708	Risk Ratio(M-H, Fixed, 95% CI)	0.69 [0.44, 1.09]

Figures

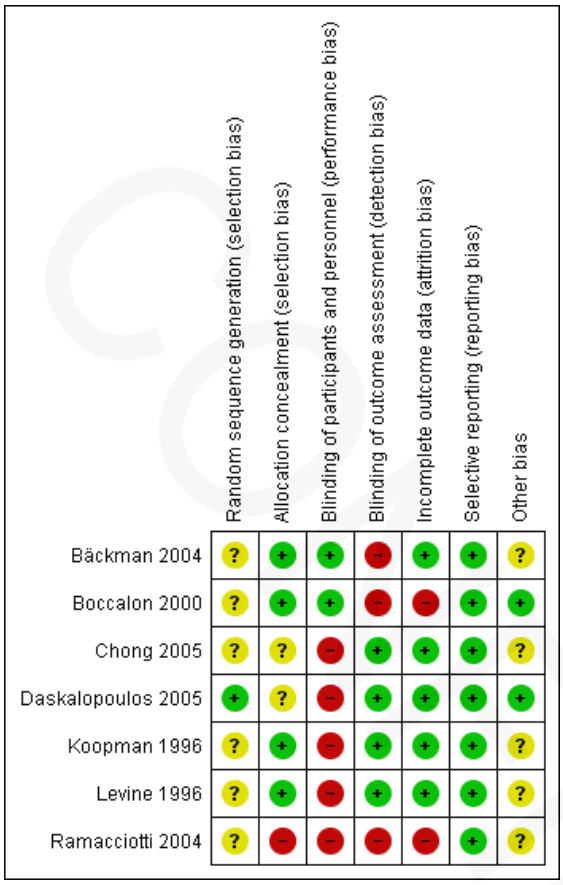
Figure 1



Caption

Study flow diagram.

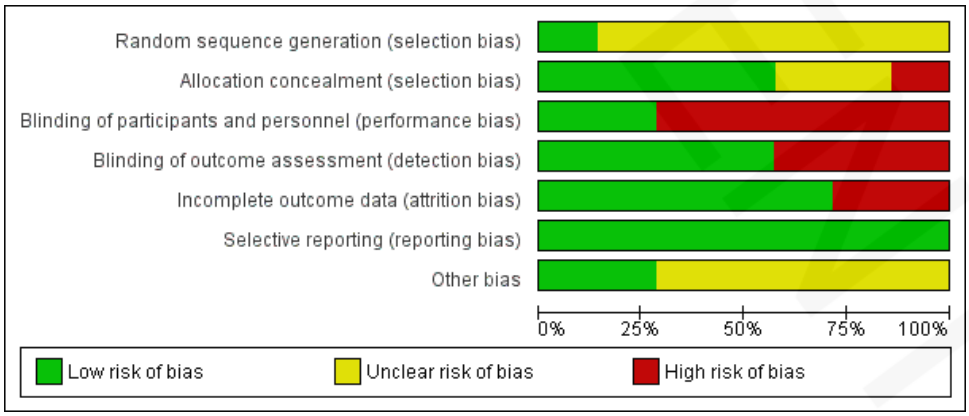
Figure 2



Caption

'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Figure 3



Caption

'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

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Internal sources

- No sources of support provided

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Feedback

1 Anticoagulant feedback, 14 February 2011

Summary

Feedback received on this review, and other reviews and protocols on anticoagulants, is available on the Cochrane Editorial Unit website at http://www.editorial-unit.cochrane.org/anticoagulants-feedback.

Reply

Contributors

Appendices

1 CENTRAL search strategy

#1	MESH DESCRIPTOR Thrombosis	1261
#2	MESH DESCRIPTOR Thromboembolism	919
#3	MESH DESCRIPTOR Venous Thromboembolism	257
#4	MESH DESCRIPTOR Venous Thrombosis EXPLODE ALL TREES	2036
#5	(thrombus* or thrombopro* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*):TI,AB,KY	18960
#6	MESH DESCRIPTOR Pulmonary Embolism EXPLODE ALL TREES	746
#7	(PE or DVT or VTE):TI,AB,KY	4979
#8	((vein* or ven*) near thromb*):TI,AB,KY	6702
#9	(blood near3 clot*):TI,AB,KY	2963
#10	(pulmonary near3 clot*):TI,AB,KY	5
#11	(lung near3 clot*):TI,AB,KY	4
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	24595
#13	MESH DESCRIPTOR Outpatients	983
#14	MESH DESCRIPTOR Inpatients	703
#15	MESH DESCRIPTOR Patient Care EXPLODE ALL TREES	48022
#16	MESH DESCRIPTOR Ambulatory Care	2843
#17	MESH DESCRIPTOR Home Nursing	253
#18	MESH DESCRIPTOR Hospitalization EXPLODE ALL TREES	10891
#19	MESH DESCRIPTOR Outpatient Clinics, Hospital	541
#20	in-patient:TI,AB,KY	4947
#21	inpatient:TI,AB,KY	5166
#22	hospitali*:TI,AB,KY	25539
#23	bed-ridden:TI,AB,KY	20
#24	bedridden:TI,AB,KY	107
#25	home:TI,AB,KY	19783
#26	out-patient:TI,AB,KY	1246
#27	outpatient:TI,AB,KY	15589
#28	ambulatory*:TI,AB,KY	14873
#29	domicil*:TI,AB,KY	383
#30	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	108891
#31	#12 AND #30	3043

2 Trials registries searches

Clinicaltrials.gov

44 studies found for: embolism AND home

WHO

809 records for 256 trials for: embolism AND home

ISRCTN

18 records for: embolism AND home

Graphs

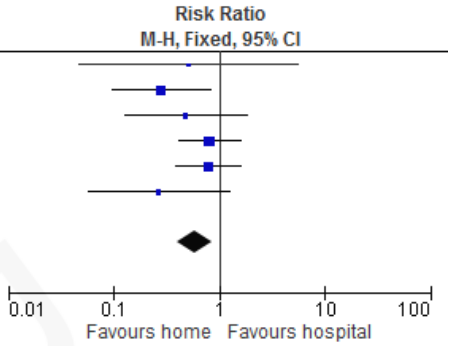
1 - Treatment of DVT at home versus treatment of DVT in hospital

1.1 Recurrence of VTE

Study or Subgroup	Treatment (Home) Events	Total	Control (Hospital) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccalon 2000	1	99	2	102	3.1%	0.52 [0.05, 5.59]
Chong 2005	4	150	14	148	22.2%	0.28 [0.09, 0.84]
Daskalopoulos 2005	3	55	6	53	9.6%	0.48 [0.13, 1.83]
Koopman 1996	14	202	17	198	27.1%	0.81 [0.41, 1.59]
Levine 1996	13	247	17	253	26.5%	0.78 [0.39, 1.58]
Ramacciotti 2004	2	104	7	97	11.4%	0.27 [0.06, 1.25]
Total (95% CI)		**857**		**851**	**100.0%**	**0.58 [0.39, 0.86]**
Total events	37		63			

Heterogeneity: Chi² = 4.35, df = 5 (P = 0.50); I² = 0%

Test for overall effect: Z = 2.70 (P = 0.007)

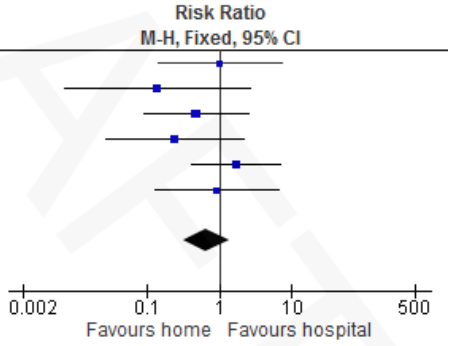


1.2 Major bleeding

Study or Subgroup	Treatment (Home) Events	Total	Control (Hospital) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccalon 2000	2	99	2	102	10.6%	1.03 [0.15, 7.17]
Chong 2005	0	150	3	148	18.9%	0.14 [0.01, 2.71]
Daskalopoulos 2005	2	55	4	53	21.9%	0.48 [0.09, 2.52]
Koopman 1996	1	202	4	198	21.7%	0.25 [0.03, 2.17]
Levine 1996	5	247	3	253	15.9%	1.71 [0.41, 7.07]
Ramacciotti 2004	2	104	2	97	11.1%	0.93 [0.13, 6.49]
Total (95% CI)		**857**		**851**	**100.0%**	**0.67 [0.33, 1.36]**
Total events	12		18			

Heterogeneity: Chi² = 4.01, df = 5 (P = 0.55); I² = 0%

Test for overall effect: Z = 1.11 (P = 0.27)

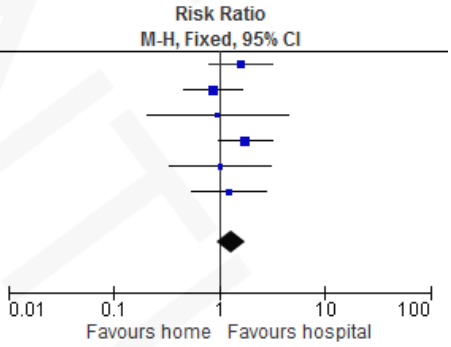


1.3 Minor bleeding

Study or Subgroup	Treatment (Home) Events	Total	Control (Hospital) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccalon 2000	17	99	11	102	17.6%	1.59 [0.79, 3.23]
Chong 2005	15	150	17	148	27.9%	0.87 [0.45, 1.68]
Daskalopoulos 2005	3	55	3	53	5.0%	0.96 [0.20, 4.56]
Koopman 1996	27	202	15	198	24.7%	1.76 [0.97, 3.21]
Levine 1996	6	247	6	253	9.7%	1.02 [0.33, 3.13]
Ramacciotti 2004	12	104	9	97	15.2%	1.24 [0.55, 2.82]
Total (95% CI)		**857**		**851**	**100.0%**	**1.29 [0.94, 1.78]**
Total events	80		61			

Heterogeneity: Chi² = 3.07, df = 5 (P = 0.69); I² = 0%

Test for overall effect: Z = 1.60 (P = 0.11)



1.4 Death

Study or Subgroup	Treatment (Home) Events	Total	Control (Hospital) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccalon 2000	0	99	2	102	5.8%	0.21 [0.01, 4.24]
Chong 2005	2	150	2	148	4.7%	0.99 [0.14, 6.91]
Daskalopoulos 2005	2	55	5	53	12.0%	0.39 [0.08, 1.90]
Koopman 1996	14	202	16	198	38.0%	0.86 [0.43, 1.71]
Levine 1996	11	247	17	253	39.5%	0.66 [0.32, 1.39]
Ramacciotti 2004	0	104	0	97		Not estimable
Total (95% CI)		**857**		**851**	**100.0%**	**0.69 [0.44, 1.09]**
Total events	29		42			

Heterogeneity: Chi² = 1.65, df = 4 (P = 0.80); I² = 0%

Test for overall effect: Z = 1.58 (P = 0.11)